

CLAIMS

What is claimed is:

1. A method of reducing an irritating or adverse side effect
5 associated with the topical ophthalmic use of an active ophthalmic drug comprising incorporating an effective amount of a cyclodextrin or cyclodextrin derivative into a formulation to complex the active drug such that the concentration of the free active drug is reduced below a tolerable threshold, and incorporating an effective amount of a viscosity increasing agent in said
10 formulation such that the bioavailability of said drug is high enough to be therapeutically effective, wherein the cyclodextrin or cyclodextrin derivative is not required to solubilize or stabilize the active drug.
2. The method of claim 1 wherein the active drug is a prostaglandin.
- 15 3. The method of claim 1 wherein the active drug is a prostamide.
4. The method of claim 1 wherein the active drug is bimatoprost.
5. The method of claim 1 wherein said irritating side effect is hyperemia.
6. A topical ophthalmic formulation comprising a therapeutically
20 active amount of an ophthalmic drug, an effective amount of a cyclodextrin or cyclodextrin derivative to complex the active drug such that the concentration of the free active drug is lowered sufficiently to significantly reduce irritating or adverse side effects, and an effective amount of a viscosity increasing agent such that the bioavailability of said active drug is high enough to be
25 therapeutically effective, wherein the cyclodextrin or cyclodextrin derivative is not required to solubilize or stabilize the active drug.
7. The topical ophthalmic formulation of claim 6 wherein the drug is bimatoprost.
8. The topical ophthalmic formulation of claim 6 which further
30 comprises an effective amount of buffer necessary to maintain the pH at about 7.3, one or more tonicity agents, and a preservative.
9. The topical ophthalmic formulation of claim 8 wherein the buffer comprises borate and the preservative is Purite®.

10. The topical ophthalmic formulation of claim 7 wherein the concentration of bimatoprost is between about 0.003% and about 0.1%.

11. The topical ophthalmic formulation of claim 7 wherein the concentration of bimatoprost is between about 0.01% and about 0.05%.

5 12. The topical ophthalmic formulation of claim 7 wherein the concentration of bimatoprost is about 0.03%.

13. The topical ophthalmic formulation of claim 7 wherein the concentration of free bimatoprost is less than about 0.02%.

10 14. The topical ophthalmic formulation of claim 7 wherein the cyclodextrin or cyclodextrin derivative is 2-hydroxypropyl β -cyclodextrin, 2-hydroxypropyl γ -cyclodextrin, or γ -cyclodextrin.

15. The topical ophthalmic formulation of claim 7 wherein the concentration of the cyclodextrin or cyclodextrin derivative is between about 0.01% and about 10%.

15 16. The topical ophthalmic formulation of claim 7 wherein the concentration of the cyclodextrin or cyclodextrin derivative is between about 0.05% and about 5%.

17. The topical ophthalmic formulation of claim 7 wherein the concentration of the cyclodextrin or cyclodextrin derivative is between about
20 0.1% and about 1.1%.

18. The topical ophthalmic formulation of claim 7 wherein the viscosity of the formulation is between about 30 centipoise and about 100 centipoise.

19. The topical ophthalmic formulation of claim 7 wherein the
25 concentration of the viscosity increasing agent is between about 0.1% and about 3%.

20. The topical ophthalmic formulation of claim 7 wherein the concentration of the viscosity agent is about 1%.

21. The topical ophthalmic formulation of claim 7 wherein the
30 viscosity agent is sodium carboxymethylcellulose or hydroxypropylmethylcellulose.

22. The topical ophthalmic formulation of claim 7 wherein the viscosity agent is sodium carboxymethylcellulose.

23. The topical ophthalmic formulation of claim 6 wherein the concentration of bimatoprost is 0.03%, which further comprises about 0.6%
5 boric acid, about 0.045% sodium borate, about 0.34% sodium chloride, about 0.14% potassium chloride, about 0.006% calcium chloride, about 0.006% magnesium chloride, and about 0.01% Purite®.

24. The topical ophthalmic formulation of claim 24 wherein the viscosity enhancing agent comprises sodium carboxymethylcellulose at a
10 concentration of about 1%.

25. The topical ophthalmic formulation of claim 24 wherein the cyclodextrin or cyclodextrin derivative comprises sodium hydroxypropyl β -cyclodextrin at a concentration between about 0.05% and about 1.1%

26. The topical ophthalmic formulation of claim 25 wherein the
15 concentration of 2-hydroxypropyl β -cyclodextrin is about 1.0%.

27. The topical ophthalmic formulation of claim 25 wherein the concentration of 2-hydroxypropyl β -cyclodextrin is about 0.08%.

28. The topical ophthalmic formulation of claim 24 wherein the cyclodextrin or cyclodextrin derivative comprises 2-hydroxypropyl γ -
20 cyclodextrin at a concentration of about 0.5%.

29. The method of claim 1 wherein the free active drug comprises between about 8% and about 90% of the active drug.

30. The method of claim 1 wherein the free active drug comprises between about 8% and about 75% of the active drug.

25 31. The method of claim 1 wherein the free active drug comprises between about 8% and about 25% of the active drug.

32. The topical ophthalmic formulation of claim 7 wherein the free active drug comprises between about 8% and about 90% of the active drug.

33. The topical ophthalmic formulation of claim 7 wherein the free
30 active drug comprises between about 8% and about 75% of the active drug.

34. The topical ophthalmic formulation of claim 7 wherein the free active drug comprises between about 8% and about 25% of the active drug.

35. A method of reducing a side effect associated with a drug administered topically to a patient's eye comprising:

(a) providing a solution of said drug in a therapeutically effective amount, which therapeutically effective amount causes said side effect;

5 (b) complexing a portion of said drug in said solution with a cyclodextrin or cyclodextrin derivative to lower the free active concentration such that the severity of said side effect is reduced; and

(c) incorporating an effective amount of a viscosity increasing agent into said solution to increase the contact time of said solution at
10 the point of administration to the eye of said patient such that the drug is delivered more effectively,

whereby the complexed portion of the drug is released over time at a rate insufficient to cause said side effect.

36. The method of claim 35 wherein the active drug is a
15 prostaglandin.

37. The method of claim 35 wherein the active drug is a prostamide.

38. The method of claim 35 wherein the active drug is bimatoprost.

39. The method of claim 35 wherein said side effect is hyperemia.

40. A topical ophthalmic formulation prepared by a process
20 comprising

(a) providing a solution of a stable and soluble drug in a therapeutically effective amount, which therapeutically effective amount causes a side effect;

(b) complexing a portion of said drug in said solution with a
25 cyclodextrin or cyclodextrin derivative to lower the free active concentration such that the severity of said side effect is reduced; and

(c) incorporating an effective amount of a viscosity increasing agent into said solution to increase the contact time of said solution at
the point of administration to the eye of said patient such that the drug is
30 delivered more effectively.

41. The formulation of claim 40 wherein the active drug is a prostaglandin.

42. The formulation of claim 40 wherein the active drug is a prostamide.
43. The formulation of claim 40 wherein the active drug is bimatoprost.
- 5 44. The formulation of claim 40 wherein said side effect is hyperemia.
45. The formulation of claim 6 wherein the active drug is a prostaglandin.
- 10 46. The topical ophthalmic formulation of claim 24 wherein the cyclodextrin or cyclodextrin derivative comprises γ -cyclodextrin at a concentration of about 0.21%.